REMARKS

Claims 1-6, 8, 10-15 and 21-23 are pending in this application. Claim 11 has been amended so as to correct an inadvertent change made to this claim in the previous Reply filed on August 29, 2003. Specifically, in the August 29th Reply Compound 158 was inadvertently deleted, even though the previous Office Action of May 29, 2003, indicated that Compounds 157 and 159 were duplicates. Therefore, Compound 158 has been re-inserted. Also, claim 11 has been amended to correctly reflect that compounds 157 and 159, as well as compounds 161 and 162, are diastereoisomeric sulfoxides of each other (i.e., isomers differing in chirality at the sulfoxide moiety) as fully supported at [1] page 8, last line to page 9, line 5, [2] page 9, lines 8-11, and [3] page 10, lines 27-30 (note especially page 10). This removes potential new issues by removing the basis for an "indefiniteness" rejection under 35 U.S.C. 112. Additionally, the definitions for formulas I and Ia have been inserted into claims 15 and 21.

It is submitted that the above-discussed changes to the claims are appropriate under 37 C.F.R. 1.116 since these changes remove potential issues under 35 U.S.C. 112 and at least place the claims into better form for appeal, should an appeal be necessary.

Removal of Rejection Under 35 U.S.C. 112, Second Paragraph

Claims 15 and 21 have been rejected under 35 U.S.C. 112, second paragraph, because these claims recite formula I and formula Ia, respectively, without providing the chemical structure of the formulas or the definitions of the substituents within the formulas. Claims 15 and 21 have been amended so as to include these missing features. It is submitted that claims 15 and 21, along with all other pending claims, comply with all requirements under 35 U.S.C. 112, second paragraph such that the above-noted rejection should be withdrawn.

Issues Under 35 U.S.C. 102(b)

Claims 1-6, 8, 10-15, 21 and 22 have been rejected under 35 U.S.C. 102(b) as being anticipated by Calverley '475 (WO 91/15475) or Calverley '629 (USP 5,374,629 which corresponds to Calverley '475).

The above-noted rejections are traversed for the following reasons.

Absence of Basis for Rejections Under 35 U.S.C. 102(b)

Calverley '475/ '629 disclose Vitamin D analogues which exhibit anti-inflammatory and immunomodulating effects. The

compounds of Calverley '475/ '629 overlap with the compounds used in the treatment method of the present invention. Calverley '475/ '629 disclose that the described compounds may be used "...in the treatment and prophylaxis of hyperparathyroidism", as well as in the treatment of other disease states, such as diabetes mellitus. This is described in the first paragraph at page 1 of Calverley '475 and in the first paragraph at column 1 of Calverley '629.

Both Calverley '475 and Calverley '629 fail to disclose or describe anywhere the use of the disclosed compounds for the treatment or prophylaxis of osteoporosis or related bone conditions, as in the treatment method of the present invention. The Calverley '475/ '629 documents fail to provide any basis for alleging "anticipation", since these documents fail to disclose all the elements of any of the claims of the present application which are all directed to the treatment and prophylaxis of osteoporosis and related bone conditions.

It appears that the Office Action may have mistakenly relied on the incorrect assumption that the disease state of hyperparathyroidism is either (1) equivalent to the disease state of osteoporosis and related bone conditions; or (2) necessarily results in osteoporosis or related bone conditions. However, the disease state of hyperparathyroidism is completely different from

the disease state of osteoporosis or related bone conditions. Although hyperparathyroidism *may* cause osteoporosis, it does not *necessarily* cause osteoporosis. Further, there are several other completely independent causes of osteoporosis (e.g., Cushing's syndrome and acromegaly) which may arise without hyperparathyroidism.

Consequently, there fails to be any adequate basis for alleging that either Calverley '475 or Calverley '629 anticipates any of the claims of the present application. Therefore, it is requested that the above-noted rejections be withdrawn.

Issues Under 35 U.S.C. 103(a)

Claims 1-6, 8, 10-15, and 21-23 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Calverley '475 and Calverley '629.

This rejection is traversed for the following reasons.

Present Invention

In the present application it was surprisingly found that compounds of the present invention show bone anabolic effects in an *in vivo* model of osteoporosis and related bone disorders demonstrated by increased boneweight and an increase in the

biomechanical strength of the bones (page 2, lines 20-21 and page 16, line 9 through page 17, line 21). It should be noted that in the *in vivo* model, the animals were ovariectomized (OVX model). In this standard osteoporosis model ovariectomy procedures alterations in the cancellous network identical to those seen in the human skeleton during ageing and the menopause (page 15, lines 11-13). The ovariectomy does not lead to excess secretion of parathyroid hormone and hyperparathyroidism induced osteoporosis.

Failure of Calverley '475/ '629 to Suggest Present Invention

The Calverley '475/ '629 documents fail to disclose or suggest the treatment method of the present invention for several reasons. First, as noted above, Calverley '475/ '629 discloses treatment for hyperparathyroidism, but states nothing whatsoever regarding osteoporosis or related bone conditions. In this regard, it is further noted that hyperparathyroidism is a disease state completely separate from osteoporosis. Hyperparathyroidism may or may not lead to osteoporosis. Additionally, osteoporosis may be caused by other completely independent conditions, such as Cushing's syndrome or acromegaly, as noted above.

Second, it is submitted that a person of ordinary skill in the art could not expect to necessarily achieve successful prophylaxis

or treatment of osteoporosis or other bone related conditions even if the compounds disclosed by Calverley '475/ '629 were successfully used to treat hyperparathyroidism. As is clear, the osteoporosis condition may arise completely independent of whether hyperparathyroidism existed or was successfully treated.

Third, the Office Action fails to provide any objective evidence which indicates a clear reason stated in Calverley '475/ '629 as to why the use of the compounds for treating hyperparathyroidism (excess secretion of parathyroid hormone) suggests that these same compounds would also be useful for treating the different disease state osteoporosis (a metabolic disorder characterized by bone resorption exceeding bone deposition). As is clear from the above discussion, the use of the compounds for successfully treating hyperparathyroidism would still fail to successfully prevent osteoporosis caused by other reasons. Further, there is no objective evidence in the present record indicating that the properties of the compounds disclosed by Calverley '475/ '629 should be expected to be effective against both hyperparathyroidism and osteoporosis. The fact that hyperparathyroidism may lead to osteoporosis falls far short of suggesting to one skilled in the art that the same compounds may be

used to treat these two different disease states which may arise based on completely different causes.

At best, the additional publications mentioned in the Office Action which mention both hyperparathyroidism and osteoporosis are evidence that it might have been "obvious to try" to experiment in order to determine if the disclosed compounds might also be useful against osteoporosis. However, this falls far short of the obviousness standard which requires a suggestion by the prior art of the invention, not merely a suggestion to experiment. In other words, there fails to be any objective evidence that there would be any reasonable expectation of success for the compounds to be useful for treating the disease state osteoporosis, based only on the fact that the compounds are useful for treating the disease state hyperparathyroidism. There is no evidence that there was a reasonable expectation of success to support a conclusion of nonobviousness. *In re Rinehart*, 189 USPQ 143 (CCPA 1976); MPEP 2143.03, page 2100-128.

In view of the above, It is submitted for the reasons stated above that the present claims define patentable subject matter such that this application should now be placed condition for allowance.

If any questions arise regarding the above matters, please contact Applicant's representative, Andrew D. Meikle (Reg. No. 32,868), in the Washington Metropolitan Area at the phone number listed below.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to March 7, 2004, in which to file a reply to the Office Action. The required fee of $110.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Andrew D. Meikle, #32,868

ADM:gmh

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000